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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/681,207

10/09/2003

Winfried Linxweiler

MERCK-2289-D01

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06/05/2006

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EXAMINER

PAK, YONG D

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/681,207

Applicant(s)

LINXWEILER ET AL.

Examiner

Yong D. Pak

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2006.
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-39 is/are pending in the application.
4a) Of the above claim(s) 27-39 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 18-26 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 09 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/9/03.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is 371 of PCT/EP00/00978, a divisional of 09/913,494.

The preliminary amendment filed on February 7, 1999, canceling claims 1-17 and adding claims 18-39, has been entered.

Claims 18-39 are pending. Claims 27-39 are withdrawn. Claims 18-26 are under consideration.

Election/Restrictions

Applicant's election with traverse of Group I (claims 18-26), in the reply filed on April 27, 2006 is acknowledged. The traversal is on the ground(s) that Yamada et al. does not disclose or suggest the method recited in claim 18. This is not found persuasive the technical feature linking Groups I-VI appears to be that they all relate to a fusion protein comprising polypeptide X and a glucose dehydrogenase. As discussed in the Restriction Requirement, Yamada et al. (form PTO-1449) discloses a fusion protein comprising a polypeptide X, alkaline phosphatase or β -galactosidase, and a glucose dehydrogenase (abstract and page 12812). Therefore, the technical feature linking the inventions of Groups I-VI does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 27-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or

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linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 27, 2006.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 9, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that the sequences in the specification, page 28 for example, lack sequence identification numbers. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 and claims 19-26 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the phrase "gene expression of polypeptide X". The metes and bounds of this phrase in the context of the above claim are not clear to the Examiner. It is not clear to the Examiner how "gene expression" of a polypeptide is detected. Examiner requests clarification of the above phrase or amend the phrase as "detecting expression of polypeptide X".

Claim 18 and claims 19-26 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the phrase "detecting presence of glucose dehydrogenase, wherein the presence of glucose dehydrogenase correlates with gene expression of polypeptide X". It is not clear to the Examiner as to how those skilled in the art can conclude that polypeptide X is indeed expressed by detecting glucose dehydrogenase. This is because applicants have not set up any control steps to account for endogenous glucose dehydrogenases present in transformants comprising the fusion protein. Therefore, the method lacks essential step(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 18-26 are drawn to a method for detecting expression of polypeptide X by expressing a fusion protein comprising glucose dehydrogenase linked with polypeptide X and detecting presence of glucose dehydrogenase, wherein presence of glucose dehydrogenase indicates expression of said polypeptide X. The claims encompass a method of using any glucose dehydrogenase isolated from any source, including any or all variants, mutants and recombinants thereof. Therefore, the claims are drawn to a method of using a genus of polypeptides having any structure. The specification only describes a method of expressing a fusion protein comprising the glucose dehydrogenase of SEQ ID NO:1 and a heterologous polypeptide, polypeptide X, and detecting presence of said glucose dehydrogenase. This is not enough and does not constitute a representative number of species to describe the whole genus of variants, recombinant and mutants of any or all glucose dehydrogenases and there is no

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evidence on the record of the relationship between the structure of the polypeptide of SEQ ID NO:1 and the structure of any or all recombinant, variant and mutant glucose dehydrogenases isolated from any source. Therefore, the specification fails to describe a representative species of the genus comprising variants, recombinants and mutants of glucose dehydrogenases used in the method to detect expression of polypeptide X.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Current Protocols in Molecular Biology et al. in view of Yamada et al. and Yamanishi et al.

Claims 18-26 are drawn to a method for detecting expression of polypeptide X by expressing a fusion protein comprising glucose dehydrogenase linked with polypeptide X and detecting presence of glucose dehydrogenase, wherein presence of glucose dehydrogenase indicates expression of said polypeptide X.

Current Protocols in Molecular Biology (form PTO-892) discloses that fusion proteins comprising a reporter protein and a protein of interest can be used to detect expression of the protein of interest by detecting the presence of the reporter protein (9.6) and a method of making fusion proteins (9.6). The reference also discloses a method of detecting a protein of interest by appending the protein with an epitope tag and detecting antibodies that recognize said epitope (10.15) and detecting proteins by staining with a silver or coomassie blue stain (Chapter 10.2). With this teaching in hand, one having ordinary skill in the art would have concluded to use proteins well

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established in the art as the reporter protein, for ease of detecting its activity or its presence.

The difference between the reference of Current Protocols in Molecular Biology and the instant invention is that Current Protocols in Molecular Biology does not teach a method of detecting expression of polypeptide X by expressing a fusion protein comprising a glucose dehydrogenase as the reporter protein and detecting presence of said glucose dehydrogenase by wherein glucose dehydrogenase activity is detected using nitro blue tetrazolium or iodophenylnotrophenyl-phenyltetrazolium salt.

Glucose dehydrogenases are well known in the art. For example, Yamada et al. discloses how to make a fusion protein comprising a heterologous protein and glucose dehydrogenase (page 12812). Even though Yamada et al. is not aimed at a method of detecting gene expression using glucose dehydrogenase as the reporter protein, Yamada et al. Does teach a method which can be used by one skilled in the art of making a fusion protein comprising a glucose dehydrogenase and a heterologous polypeptide. Further, ExPASY (form PTO-892) summarizes a list of known glucose dehydrogenases.

Also, detection of glucose dehydrogenase activity by assaying for its activity using a terazolium salt is well known in the art. Yamanishi et al. (US 4,622,296 – form PTO-892) discloses a method of detecting glucose dehydrogenase by incubating a gel comprising the dehydrogenase with nitro blue tetrazolium or iodophenylnotrophenyl-phenyltetrazolium (Column 4).

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Therefore, combining the teachings of Current Protocols in Molecular Biology Yamada et al. and Yamanishi et al., it would have been obvious to one having ordinary skill in the art to detect expression of a heterologous protein by expressing a fusion protein comprising the heterologous protein and a reporter protein, such as a glucose dehydrogenase, by detecting presence of the reporter by detecting antibodies raised against said reporter protein, assaying for activity of the reporter protein using tetrazolium salts and detecting presence of the reporter protein with a silver or coomassie blue stain. One of ordinary skill in the art would have been motivated to use glucose dehydrogenase as the reporter protein because the protein can be easily assayed. One of ordinary skill in the art would have had a reasonable expectation of success since Current Protocols in Molecular Biology teaches how to make fusion proteins and assaying for reporter protein activity, Yamada et al. teaches how to make a fusion protein comprising glucose dehydrogenase and a heterologous protein and Yamanishi et al. teaches how to measure activity of glucose dehydrogenase using tetrazolium salts.

Therefore, the above references render claims 18-26 *prima facie* obvious to one of ordinary skill in the art.

None of the claims are allowable.

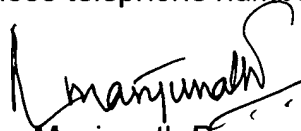
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

A handwritten signature in black ink, appearing to read "Manjunath Rao", with a stylized flourish at the end.

Manjunath Rao
Primary Patent Examiner 1652